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Interventions (other than psychosocial, psychological and pharmacological) for treating postpartum depression (Protocol)

Dennis CL, Brown JVE, Brown HK

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Interventions (other than psychosocial, psychological and pharmacological) for treating postpartum depression.
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[Intervention Protocol]

Interventions (other than psychosocial, psychological and pharmacological) for treating postpartum depression

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ABSTRACT

This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:

The primary objective of this review is to assess the effects, on mothers and families, of interventions (other than psychosocial, psychological and pharmacological) compared with usual care in postpartum depression.

Secondary objectives are to examine the effectiveness of:

1. specific types of physical therapies (e.g. bright light therapy, physical exercise, yoga, acupuncture, sleep deprivation);
2. specific types of nutraceuticals (e.g. omega-3 fatty acids);
3. specific types of herbal remedies (e.g. St. John's Wort).

BACKGROUND

Description of the condition

Depression is common in the perinatal period and is linked to negative consequences for women and their families, including long-term adverse outcomes in children (Stein 2014). In a landmark meta-analysis of 59 studies, 13% of women were found to have experienced major depressive symptoms at some point during the first 12 weeks following childbirth (number of women = 12,810) (O'Hara 1996). A more recent systematic review found that the period prevalence of major and minor depressive symptoms was 19.2% in the first 12 weeks postpartum, with a period prevalence of 7.1% for a major depressive disorder (Gaynes 2005). Depression appears to be more common in low- and middle-income countries than in high-income countries, with reported rates of up to 20% in postpartum women (Fisher 2012). Approximately 26.5% of women with postpartum depression report episode onset before pregnancy (Wisner 2013), which highlights preconception care as an important management strategy.

Common symptoms of postpartum depression include emotional lability (exaggerated changes in mood or affect in quick succession), dysphoria (unease or dissatisfaction), confusion, insomnia, and guilt. Anxiety is also a frequent symptom; meta-analytic data suggest that within the first six months postpartum, the prevalence of coexisting anxiety and depressive symptoms is 8.2% (15 studies; number of women = 14,731) (Falah-Hassani 2017). The course of postpartum depression is variable and depends on a multitude of factors, including: a woman's prior depressive history, the persistence versus resolution of stressors contributing to the depressive episode, the severity of symptoms, and whether a woman seeks appropriate treatment. While some postpartum depression will resolve spontaneously within a few weeks, approximately 20% of episodes persist beyond the first year, and up to 40% of women will experience a relapse of their depression (Goodman 2004).

Description of the intervention

Recommended treatment for postpartum depression depends on factors related to a woman's specific presentation, including severity of the current depressive episode, risk assessment, comorbidities, psychiatric history (e.g. severity of prior depressive episodes), social stressors, social supports, and patient preference. Stepped-care approaches, in which treatment options escalate in intensity based on symptom severity and patient response, can be implemented collaboratively.

The most commonly used treatments for depression are antidepressants, psychotherapy, or a combination of the two. While both treatment strategies (alone and in combination) have been shown to be effective, more recent meta-analyses have found high rates of dropout and low rates of remission (Haller 2019). While pharmacotherapy is a frequent treatment choice for moderate to severe depression, postpartum women are often hesitant to take antidepressants due to concerns about transmission to the infant through breast milk (Dennis 2006). A Cochrane Review evaluated psychological therapies (such as cognitive-behavioural therapy and interpersonal psychotherapy), as well as psychosocial interventions (e.g. non-directive counselling, nurse/midwife home visits, peer support), for the treatment of postpartum depression (Dennis 2007). The review found that both psychological and psychosocial interventions were effective in reducing depressive symptomatology. Recent treatment guidelines — including those from the National Institute for Health and Care Excellence (NICE, UK), the Canadian Network for Mood and Anxiety Treatments (CANMAT, Canada), and Beyond Blue (Australia) — support the importance of these interventions (Austin 2011; McQueen 2016; NICE 2014).

There are, however, a number of reasons why psychological therapy and psychosocial interventions may not be an option. Psychological therapy may not be effective on its own for treating severe depression. It can also be difficult for a new mother to attend psychological therapy or a psychosocial programme, due to time constraints and the need to organise childcare. Furthermore, some women — including those living in rural or remote areas — may have limited access to treatment due to a lack of transportation, geographical distance, or the unavailability of a trained provider. Interventions other than those which are pharmacological, psychosocial or psychological are also available for treating depression. These "alternative" treatments, which include mind and physical body therapies and herbal remedies, are often considered because of the prevalent belief that "natural is better" (Ravindran 2009).

How the intervention might work

There are several alternative treatment options available for depression. These include mind and physical body practices (e.g. bright light therapy, physical exercise, yoga, acupuncture, sleep deprivation, repetitive transcranial magnetic stimulation, transcranial direct current stimulation), nutraceuticals (e.g. omega-3 fatty acids), and herbal remedies (e.g. St. John's Wort).

Mind and physical body practices

Bright light therapy typically consists of exposure to a 10,000 lux (intensity) fluorescent light box for 30 minutes per day, often in the early morning at home. Response usually occurs within three weeks. The mechanism of action, though still unclear, is thought to be through correcting disturbed circadian rhythms and improving the regulation of chemical and neurotransmitter pathways (e.g. serotonin and catecholamine systems) (Crowley 2012; Sohn 2005).

Another treatment option is physical exercise, where programmes are usually delivered over eight to 20 weeks (average: 12 weeks), three times per week for 30 to 60 minutes per session. The mechanisms explaining the impact of various forms of physical exercise on depression are not well understood. However, it is hypothesized that the effect is explained by both psychological and neurobiological factors. Psychological factors include increased sense of self-efficacy and mastery as well as distraction from stress. Exercise is also thought to impact complex biological and neural pathways (Strohle 2009).

Yoga is a physical therapy which integrates body postures, meditation, and breath control. It is typically practiced over four to eight weeks, usually four times a week, for 45 to 60 minutes per session (Ravindran 2009).

In acupuncture, special needles are used to pierce the skin surface at specific points on the body to produce particular therapeutic effects. Treatment usually lasts four to eight weeks; there is wide variation in the number of needles (two to 16) and sessions used. It is believed that acupuncture stimulates nerve fibres which then trigger the central immune system and induce the release of neu-

rotransmitters (e.g. serotonin, norepinephrine, dopamine, and endorphins) (Wang 2008).

Sleep deprivation involves keeping patients awake for long (40-hour) or short (three- to four-hour) periods of time. One to six cycles are usually used over four weeks (Ravindran 2009). Sleep deprivation is thought to impact on depression through complex biological processes such as the hypothalamic-pituitary adrenal axis, or circadian rhythms (Ravindran 2009).

Emerging non-invasive, localized brain-stimulation therapies for depression, that pose no theoretical risk to a developing fetus, are increasingly being investigated for use in the perinatal population. These include repetitive transcranial magnetic stimulation (rTMS), which uses magnetic coils (typically targeted at the dorsolateral prefrontal cortex) to modulate activity (Downar 2013), and transcranial direct current stimulation (tDCS), which uses low-intensity direct current via electrodes placed to modulate regional brain activity in the prefrontal cortex (Vigod (in press)).

Nutraceuticals

Nutraceuticals are non-prescription natural health products. They typically take the form of concentrated, naturally occurring substances such as vitamins and minerals (e.g. omega-3 fatty acids, S-Adenosylmethionine (SAM-e), tryptophan, inositol, folic acid, amino acids, alpha-lactabumin, dehydroepiandrosterone (DHEA), and acetyl-L-carnitine) (Ravindran 2009). These are used alone or in combination to promote general well-being. Omega-3 fatty acids, for example, are polyunsaturated fatty acids found in multiple biological systems. They have been studied in different doses and formulations (e.g. cetyl esters of eicosapentanoic acid (EPA) or docosahexaenoic acid (DHA), or a combination of both). Omega-3 fatty acids are thought to be associated with processes such as increased serotonergic neurotransmission, regulation of corticotropin-releasing factor, and alterations in dopamine function (Freeman 2006); however, their mechanisms are not fully understood (Freeman 2011). Folate, which is involved in complex pathways that comprise the one-carbon cycle, is thought to impact depression by affecting synthesis of neurotransmitters such as serotonin, dopamine, and norepinephrine (Freeman 2010).

Herbal remedies

Another sub-category of natural health products, herbal remedies are derived from plants and plant extracts such as flowers, leaves, roots, bark and berries. Herbal remedies are sold as non-prescription products (Ravindran 2009). Examples are St. John's wort (*Hypericum perforatum*), *Gingko biloba*, *Crocus sativus*, *Lavandula angustifolia*, and *Rhodiola rosea*, to name a few. The mechanism of action for herbal remedies is poorly understood. For example, St. John's wort, one of the most common herbal remedies for depression, may operate through several pathways. There is some evidence to suggest that it may inhibit uptake of serotonin, norepinephrine, and dopamine. Other evidence suggests a role for regulation of genes that control the hypothalamic-pituitary-adrenal axis (Butterweck 2003).

Why it is important to do this review

Postpartum depression occurs during a period when the infant is highly dependent on parental care and is very sensitive to the quality of the interaction. Concern for child development is warranted as postpartum depression can interfere with good parenting interactions and can cause substantial stress for children. The ever-growing literature clearly suggests that maternal depression adversely affects infant development (Stein 2014). In observational studies, infants of depressed mothers, compared with those of non-depressed mothers, have been shown to be more fussy, score more poorly on measures of intellectual and motor development, have less secure attachments to their mothers and more difficult temperaments, show delayed development of self-regulatory strategies, react more negatively to stress, and exhibit poorer academic performance, lower levels of self-esteem, fewer social competencies, and higher levels of behavioural problems (England 2009; Goodman 1999). A meta-analysis of 193 studies reported that maternal depression (not restricted to the postpartum period) was associated with higher levels of general psychopathology, internalising behaviour, externalising behaviour, and lower levels of positive affect in the child (Goodman 2011). Of particular importance is the observation that these effects were stronger if exposure to maternal depression occurred when the child was at an early age. There are several possible mechanisms by which maternal interactions may transmit risk from the depressed mother to the child; these include maternal modelling of depressed affect, behaviours, and cognitions; inconsistent discipline practices; reduced positive reinforcement for the child; and the development of an insecure child attachment. Maternal depression may also have an indirect effect through its detrimental impact on the marital relationship and family functioning. International experts have clearly identified maternal depression as a major adversity for children and effective interventions to address this condition are one of the most important public health strategies to reduce the long-term adverse developmental effects on children. This Cochrane Review will provide evidence of the effectiveness of currently available alternative treatments for postpartum depression and may provide a rationale for the development of new and innovative treatments. As such, it will aid in the prevention of poor child developmental outcomes. In addition, a survey of primary care patients showed that, among people with depression and anxiety, approximately the same proportion (11%) report using complementary or alternative medicine therapy (Roy-Byrne 2005), as those who use anti-depressant medication (Mojtabai 2008). While this is an older survey, it does suggest individuals are using alternative therapies at an increasing rate, and so information about their effectiveness for the treatment of postpartum depression is needed.

Three existing Cochrane Reviews are important to note in this context. One of these evaluated the effect of psychosocial and psychological interventions for the treatment of postpartum depression (Dennis 2007). In an analysis of ten trials, the authors found that any psychosocial or psychological intervention, compared to usual postpartum care, was associated with a reduction in the risk of continued postpartum depression. This reduction was maintained at the final assessment within the first year postpartum. The effect was consistent across type of intervention (psychosocial or psychological) and type of diagnosis at entry into the trial (clinical or self-report of depressive symptomatology). The second review assessed the effectiveness of antidepressants for treating postpartum depression (Molyneaux 2014). The authors included six trials: four evaluated the effectiveness of selective serotonin reuptake inhibitors (SSRIs) relative to placebo, one compared sertraline and nortriptyline, and one compared any antidepressant to treatment as usual. The authors found that SSRIs were significantly more effective than placebo for treating women with postpartum depression. However, the authors were unable to determine

whether some antidepressants were more effective than others. The third review, Dennis 2008, evaluated the effect of oestrogens and progestins in preventing and treating postpartum depression. Only two trials met the study inclusion criteria. The one treatment trial suggested oestrogen may be effective in reducing depression scores among women who had severe depression. There is currently a gap in the evidence regarding the effect of other interventions (e.g. physical therapies, nutraceuticals, and herbal remedies) in the treatment of postpartum depression. This review will aim to synthesize the available evidence on these interventions, and identify areas for research

OBJECTIVES

The primary objective of this review is to assess the effects, on mothers and families, of interventions (other than psychosocial, psychological and pharmacological) compared with usual care in postpartum depression.

Secondary objectives are to examine the effectiveness of:

1. specific types of physical therapies (e.g. bright light therapy, physical exercise, yoga, acupuncture, sleep deprivation);
2. specific types of nutraceuticals (e.g. omega-3 fatty acids);
3. specific types of herbal remedies (e.g. St. John's Wort).

METHODS

Criteria for considering studies for this review

Types of studies

We will include all published, unpublished and ongoing randomized controlled, cluster-randomized controlled, and cross-over trials of interventions (other than psychosocial, psychological and pharmacological) in which the primary or secondary aim is the reduction in postpartum depression. We will exclude quasi-randomized trials (e.g. those randomized by delivery date, or odd versus even medical record numbers) from the analysis.

Types of participants

The study participants will include women of all ages who developed depression up to 12 months postpartum, who were identified with either:

1. depressive symptomatology using cut-off scores on self-report measures, e.g. the Edinburgh Postnatal Depression Scale (EPDS) (Cox 1987), the Beck Depression Inventory (BDI) (Beck 1961); or
2. clinical depression using a diagnostic interview, e.g. Structured Clinical Interview for DSM-IV (SCID) (Spitzer 1992).

We will accept all comorbidities, including mental and physical conditions, as long as depression was the main focus of the trial. We will include studies in which participants were recruited from diverse settings, including hospital clinics, primary care, and in-home. Where studies used self-report measures of depression, we will use the threshold scores for the respective scales as applied by the investigators in the trials.

Types of interventions

Experimental interventions

Interventions will include:

1. Mind and physical body practices (e.g. bright light therapy, physical exercise, yoga, acupuncture, sleep deprivation);
2. Nutraceuticals (e.g. omega-3 fatty acids);
3. Herbal remedies (e.g. St. John's Wort).

We will include interventions that can be delivered on an individual or group basis during the postpartum period, either in-home, during clinic visits, or by telephone (e.g. for physical exercise interventions), by either a healthcare professional (e.g. nurse, midwife, childbirth educator, physician, psychiatrist, psychologist) or lay person (e.g. a specially trained person from the community, student, research assistant). Studies will only be eligible for inclusion if treatment was initiated postpartum. We will exclude studies in which treatment started during pregnancy, even if postpartum depression outcomes were reported. Interventions can range in frequency, duration, and dosage. Interventions other than the ones listed here as examples will be eligible for inclusion provided they cannot be more reasonably characterized as psychosocial, psychological, or pharmacological.

Comparator interventions

Standard or usual care: this includes any appropriate healthcare received during the course of the trial, including pharmacotherapy (e.g. antidepressants), as deemed necessary by the clinician. We will exclude trials which evaluate one treatment against another treatment.

Types of outcome measures

Studies that meet the above criteria will be included regardless of whether they report on the following outcomes.

Primary outcomes

1. Postpartum depression (as variously defined and measured by trialists, including above a self-reported cut-off or a clinical diagnosis (dichotomous) and depression severity (continuous))
2. Adverse events or outcomes (variously defined, dichotomous)
   a. For the mother (e.g., nausea, diarrhoea, headaches)
   b. For the breastfeeding infant (eg., poor sleep, feeding problems, diarrhoea)

Secondary outcomes

Maternal

1. Maternal-infant attachment (e.g. Strange Situation (Ainsworth 1978), dichotomous or continuous)
2. Anxiety (e.g. State-Trait Anxiety Inventory (Spielberger 1970), dichotomous or continuous)
3. Maternal stress (e.g. Perceived Stress Scale (Cohen 1983), dichotomous or continuous)
4. Parenting stress (e.g. Parenting Stress Index (Abidin 1983), dichotomous or continuous)
5. Maternal perceived social support (e.g. Social Provisions Scale (Cutrona 1987), dichotomous or continuous)
6. Maternal dissatisfaction with intervention (variously defined, dichotomous or continuous)

Infant

1. Infant developmental assessments (e.g. Ages and Stages Questionnaire (Squires 1999), dichotomous or continuous)

Family

1. Marital discord (e.g. Dyadic Adjustment Scale (Spanier 1976), dichotomous or continuous)

Timing of outcome assessment

For all comparisons, we will classify outcomes as (1) assessment carried out immediately post-treatment, and (2) final assessment carried out within the first year postpartum. Our primary time point will be the assessment carried out immediately post-treatment. If the study includes multiple assessments from the post-treatment period up to one year postpartum, we will include the last follow-up assessment.

Hierarchy of outcome measures

Where studies include multiple measures of the same outcome, we will include in data analysis the most commonly used measure. For example, for self-reported measures of postpartum depression (e.g. the Edinburgh Postnatal Depression Scale (EPDS) (Cox 1987) and Hamilton Rating Scale for Depression (HRSD) (Hamilton 1960)), we will use the EPDS. Where the authors include both clinician-administered scales and self-report measures, we will include in data analysis the clinician-administered scale.

Search methods for identification of studies

Cochrane Common Mental Disorders Controlled Trials Register (CCMDCTR)

The Cochrane Common Mental Disorders Group (CCMD) maintains two archived clinical trials registers at its editorial base in York, UK: a references register and a studies-based register. The CCMDCTR-References Register contains over 40,000 reports of randomized controlled trials (RCTs) in depression, anxiety and neurosis. Approximately 50% of these references have been tagged to individual, coded trials. The coded trials are held in the CCMDCTR-Studies Register and records are linked between the two registers through the use of unique Study ID tags. Coding of trials is based on the EU-Psi coding manual, using a controlled vocabulary; (please contact the CCMD Information Specialists for further details). Reports of trials for inclusion in the Group's registers are collated from routine (weekly), generic searches of MEDLINE (1950 to 2016), Embase (1974 to 2016) and PsycINFO (1967 to 2016); quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL) and review-specific searches of additional databases. Reports of trials are also sourced from international trial registers via the World Health Organization's trials portal (the International Clinical Trials Registry Platform (ICTRP)), pharmaceutical companies, the handsearching of key journals, conference proceedings and other (non-Cochrane) systematic reviews and meta-analyses.

Further details of CCMD's core search strategies (used to identify RCTs for their specialized register) can be found on the Group's website, for transparency they are also summarized in Appendix 1. The CCMDCTR is current to June 2016.

Electronic searches

1. Cochrane Specialized Registers

Common Mental Disorders Group

The CCMDCTR will be searched using the following strategies.
CCMDCTR-Studies
(Diagnosis = "Depression, Postpartum") or (Diagnosis = Depress* and Comorbid Diagnosis= Pregnan*)

CCMDCTR-References will be searched using a more sensitive set of terms to identify additional reports of RCTs not yet tagged to individual studies:
((depress* NEAR (postpartum* or post-partum* or "post partum" or postnatal* or post-natal* or "post natal" or puerp* or perinatal* or peri-natal* or "peri natal*" or peripartum* or peri-partum* or "peri partum*" or pregnan* or maternal*)) or (baby-blue* or "baby blue*")):ti,ab,ky,kw,emt,mh

Cochrane Pregnancy and Childbirth Group

A search of the Cochrane Pregnancy and Childbirth Group (PCG) Trials Register will also be conducted. This register also contains relevant RCTs from MEDLINE, Embase, PsycINFO and CENTRAL (further details available on the PCG website).

There will be no restrictions on date, language or publication status applied to the searches.

2. International Trial Registries

International trial registries will be searched via the World Health Organization's trials portal (ICTRP) and ClinicalTrials.gov to identify unpublished or ongoing studies.

3. Biomedical Databases

Additional searches will be conducted on Ovid MEDLINE, PsycINFO and the Cochrane Library (2016 onwards) to cover the period when the CCMDCTR fell out of date with the editorial group's move from Bristol to York. (Embase is already covered by CENTRAL and the PCG register).

Searching other resources

Reference lists

For references lists, we will conduct forward and backward citation tracking of all included studies to identify additional studies missed from the original electronic searches (e.g. unpublished or in-press citations). We will not apply any language restrictions.

Correspondence

We will make contact with experts in the field to request additional trial data or information on unpublished or ongoing studies.

Data collection and analysis

Selection of studies

Two review authors (JVEB and HKB) will independently assess for inclusion all the potential studies we identified as a result of the search strategy. After assessing titles and abstracts, we will retrieve full-text articles for potentially eligible studies. We will then include and exclude studies according to the methods described above. We will resolve any uncertainties regarding the appropriateness for inclusion through discussion or consultation with a third review author (CLD). We will exclude duplicate studies and record reasons for exclusion or ineligible studies (outlined in the 'Characteristics of excluded studies' table). We will collate multiple reports related to the same study so that each study rather than each report will be the unit of interest in the review. We will record the selection process

in sufficient detail to complete a PRISMA flow diagram and 'Characteristics of included studies' table.

Data extraction and management

We will use a previously designed data extraction form to collect study characteristics related to trial methods (method of allocation generation, method of allocation concealment, loss of participants to follow-up, blinding, use of intention-to-treat analysis), inclusion and exclusion criteria for participants, details of the intervention and control groups, as well as outcome data (number of events and total number of participants or means and standard deviations for intervention and control groups, as relevant). For eligible studies, two review authors will independently extract the data using the agreed form. We will resolve discrepancies through discussion or, if required, we will consult a third person. We will enter data into Review Manager 5 software or RevMan Web (Review Manager 2014; RevMan Web 2019), and check for accuracy by comparing the data presented in the systematic review with the study reports. When information regarding any of the above is unclear, we will attempt to contact authors of the original reports to provide further details.

Main planned comparisons

We will make the following treatment comparisons.

1. All physical therapies versus standard care or usual care
2. All nutraceuticals versus standard care or usual care
3. All herbal remedies versus standard care or usual care

Data permitting, we will conduct subgroup analyses by individual treatment type.

Assessment of risk of bias in included studies

Two review authors will independently assess risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We will resolve any disagreements by discussion or by involving another author. For the following domains, we will judge each study to be at "high", "low", or "unclear" risk of bias, using quotes from the trial publication to support our assessment.

1. Sequence generation (checking for possible selection bias)
2. Allocation concealment (checking for possible selection bias)
3. Blinding of participants and personnel (checking for possible performance bias)
4. Blinding of outcome assessors (checking for possible detection bias)
5. Incomplete outcome data (checking for possible attrition bias through withdrawals, dropouts, protocol deviations)
6. Selective reporting bias
7. Other sources of bias

For cluster-randomized trials, we will describe the following (in accordance with the *Cochrane Handbook*, section 16.3.2 Higgins 2011).

1. Recruitment bias: whether the individuals participating in the trial were blinded to the type of cluster they were in before agreeing to participate
2. Baseline imbalances: whether there were differences in baseline characteristics between the randomized groups
3. Loss of clusters: whether any complete clusters were lost to follow-up and the reasons
4. Incorrect analysis: whether the proper statistical analysis was carried out for a cluster-randomized design
5. Differences in intervention effects: whether the cluster randomization method could have resulted in different intervention effects than an individually-randomized trial

With reference to (1) to (6) above, we will assess the likely magnitude and direction of the bias and whether we consider it to be likely to impact on the findings. We will explore the impact of the level of bias through undertaking sensitivity analyses; see Sensitivity analysis.

Measures of treatment effect

Dichotomous data

For dichotomous data, we will present results as summary risk ratio (RR) with 95% confidence intervals (CIs).

Continuous data

For continuous data, we will use the mean difference if outcomes were measured in the same way between trials. We will use the standardized mean difference (SMD) to combine trials that examined the same outcome, but used different measures.

Unit of analysis issues

Cluster-randomized studies

We will include cluster-randomized trials in the analyses along with individually-randomized trials. We will adjust the sample sizes using the methods described in section 16.3.4 of the *Cochrane Handbook*, using an estimate of the intracluster correlation coefficient (ICC) derived from the trial. If there is little heterogeneity between the study designs, we will synthesize the relevant information from the cluster-randomized trials and individually-randomized trials we identify.

We will also acknowledge heterogeneity in the randomization unit and will perform a sensitivity analysis to investigate the effects of the randomization unit.

Studies with multiple treatment groups

We will include studies with multiple treatment arms. We will describe all treatment arms in the 'Characteristics of studies' tables. For the meta-analysis, we will combine groups to conduct a single pair-wise comparison, where possible. We will also combine control arms if there is more than one that meets criteria for ‘standard care’.

Dealing with missing data

For included studies, we will contact study authors for missing data. We will note levels of attrition. We will explore the impact of including studies with high levels of missing data in the overall assessment of treatment effect by using sensitivity analysis. We will compare those trials where 80% of data on a given outcome were available for those who were originally randomized versus those with less than 80%. For all outcomes, we will carry out analyses, as far as possible, on an intention-to-treat basis, i.e. we will attempt to include all participants randomized to each group in the analyses, and all participants will be analyzed in the group to which they

were allocated, regardless of whether or not they received the allocated intervention. The denominator for each outcome in each trial will be the number randomized minus any participants whose outcomes are known to be missing. It is important to note that if data remain missing after attempts to obtain them, for some measures of variation where there is an approximate or direct algebraic relationship with the standard deviation, it may be possible to obtain the required statistic even if it is not published in the paper, as explained in the *Cochrane Handbook*, sections 7.7.3.2 to 7.7.3.7. We will closely examine our missing data and determine if imputations are possible.

Assessment of heterogeneity

We will assess statistical heterogeneity visually by studying the degree of overlap of the CIs for individual studies in a forest plot. We will also carry out more formal assessments using the t^2, I^2 and Chi^2 statistics. We will regard heterogeneity as substantial if t^2 is greater than zero or if there is a low P value (less than 0.10) in the Chi^2 test for heterogeneity. We will interpret the I^2 value in accordance with the *Cochrane Handbook* (Higgins 2011), as follows:

1. 0% to 40%: might not be important;
2. 30% to 60%: may represent moderate heterogeneity;
3. 50% to 90%: may represent substantial heterogeneity;
4. 75% to 100%: considerable heterogeneity.

Assessment of reporting biases

For the primary outcome (postpartum depression), if there are 10 or more studies in the meta-analysis, we will investigate possible reporting biases (such as publication bias) using funnel plots. We will assess funnel plots visually, and if there is any obvious asymmetry apparent (often attributed to publication bias) we will seek statistical advice on carrying out formal tests for funnel plot asymmetry.

Data synthesis

We will carry out statistical analysis using Review Manager 5 software (Review Manager 2014). We will use fixed-effect meta-analysis for combining data where it is reasonable to assume that the studies are estimating the same underlying treatment effect, i.e. where trials examine similar interventions, and the trials' populations and methods are judged to be sufficiently similar. If there is clinical heterogeneity sufficient to expect that the underlying treatment effects differ between trials, or if substantial statistical heterogeneity is detected, we will use random-effects meta-analysis to produce an overall summary if an average treatment effect across trial is considered clinically meaningful. The random-effects summary will be treated as the average range of possible treatment effects and we will consider the clinical implications of treatment effects differing between trials. If the average treatment effect is not clinically meaningful we will not combine trials. If we use random-effects analyses, the results will be presented as the average treatment effect with its 95% confidence interval, and the estimates of t^2 and I^2. We will not use the random-effects model as a primary analysis if less than five studies are included in this review.

Subgroup analysis and investigation of heterogeneity

We plan to complete a priori subgroup analyses to investigate the effect of:

1. type of specific physical therapy (e.g. bright light therapy, physical exercise, yoga, acupuncture, sleep deprivation);
2. type of nutraceuticals (e.g. omega-3 fatty acids);
3. type of herbal remedies (e.g. St. John's Wort).
4. intervention mode (e.g. individually-based physical therapy interventions, group-based physical therapy interventions);
5. sample selection criteria (e.g. women selected based on clinically diagnosed depression versus self-reported depression).

Where data are available, we will conduct subgroup analyses for our primary outcome:

Postpartum depression (as variously defined and measured by trialists, including above a self-reported cut-off or a clinical diagnosis (dichotomous) and depression severity (continuous))

For random-effects and fixed-effect meta-analyses, we will assess differences between subgroups by inspection of the subgroups' confidence intervals; non-overlapping confidence intervals suggest a statistically significant difference in treatment effect between the subgroups. We will also carry out formal subgroup analyses, available in Review Manager 5 (Review Manager 2014).

Sensitivity analysis

We plan to conduct sensitivity analyses, for the primary outcomes, in instances in which there was a high risk of bias due to any of the following:

1. inadequate allocation concealment;
2. unblinded outcome assessment or outcome assessment uncertain;
3. incomplete outcome data (more than 20% missing data) for any of the included trials.

These sensitivity analyses will involve removing studies with high and unknown risk of bias and we will only undertake them where there is an adequate number of studies.

Summary of findings

We will use the GRADE approach (Schunemann 2009) to evaluate the quality of the available evidence. We will create 'Summary of findings' tables using GRADEpro GDT software (GRADEPro GDT 2015). We will import data from Review Manager 5 into GRADEpro GDT. Tables will then be generated that provide information about: (1) the overall quality of the available evidence for each specific outcome, (2) the magnitude of the effect of the intervention, and (3) the sum of the available data on each outcome. We will assess the quality of the available evidence based on the following five considerations:

1. limitations in study design;
2. indirectness of evidence;
3. heterogeneity of results;
4. imprecision of effect estimates;
5. publication bias.

We will classify the quality of evidence for each outcome that includes pooled data as follows:

1. high quality (further research will not likely change our confidence in the effect estimate);

2. moderate quality (further research will likely impact our confidence in the effect estimate);
3. low quality (further research will very likely impact our confidence in the effect estimate);
4. very low quality (we are very uncertain about the effect estimate).

We will downgrade the quality rating by one level for serious issues and by two levels for very serious issues. Our 'Summary of findings' tables will include the following outcomes, measured immediately post-treatment, for the main comparisons (intervention versus standard care):

1. postpartum depression;
2. anxiety;
3. maternal stress;
4. parental stress;
5. maternal perceived social support.

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APPENDICES

Appendix 1. CCMDCTR core search strategies

The core search strategies used to identify reports of RCTs for the Cochrane Common Mental Disorders Specialised Register (CCMD-CTR), are listed below.

OVID MEDLINE (1950 to date): 1. eating disorders/ or anorexia nervosa/ or binge-eating disorder/ or bulimia nervosa/ or female athlete triad syndrome/ or pica/ 2. hyperphagia/ or bulimia/ 3. self-injurious behavior/ or self mutilation/ or suicide/ or suicidal ideation/ or suicide, attempted/ 4. mood disorders/ or affective disorders, psychotic/ or bipolar disorder/ or cyclothymic disorder/ or depressive disorder/ or depression, postpartum/ or depressive disorder, major/ or depressive disorder, treatment-resistant/ or dysthymic disorder/ or seasonal affective disorder/ 5. neurotic disorders/ 6. depression/ 7. adjustment disorders/ 8. exp antidepressive agents/ 9. anxiety disorders/ or agoraphobia/ or neurocirculatory asthenia/ or obsessive-compulsive disorder/ or obsessive hoarding/ or panic disorder/ or phobic disorders/ or stress disorders, traumatic/ or combat disorders/ or stress disorders, post-traumatic/ or stress disorders, traumatic, acute/ 10. anxiety/ or anxiety, castration/ or koro/ 11. anxiety, separation/ 12. panic/ 13. exp anti-anxiety agents/ 14. somatoform disorders/ or body dysmorphic disorders/ or conversion disorder/ or hypochondriasis/ or neurasthenia/ 15. hysteria/ 16. munchausen syndrome by proxy/ or munchausen syndrome/ 17. fatigue syndrome, chronic/ 18. obsessive behavior/ 19. compulsive behavior/ or behavior, addictive/ 20. impulse control disorders/ or firesetting behavior/ or gambling/ or trichotillomania/ 21. stress, psychological/ or burnout, professional/ 22. sexual dysfunctions, psychological/ or vaginismus/ 23. anhedonia/ 24. affective symptoms/ 25. *mental disorders/ 26. (eating disorder* or anorexia nervosa or bulimi* or binge eat* or (self adj (injur* or mutilat*)) or suicide* or suicidal or parasuicid* or mood disorder* or affective disorder* or bipolar i or bipolar ii or (bipolar and (affective or disorder*)) or mania or manic or cyclothymic* or depression or depressive or dysthymi* or neurotic or neurosis or adjustment disorder* or antidepress* or anxiety disorder* or agoraphobia or obsess* or compulsi* or panic or phobi* or ptsd or posttrauma* or post trauma* or combat or somatoform or somati#ation or medical* unexplained or body dysmorphi* or conversion disorder or hypochondria* or neurastheni* or hysteria or munchausen or chronic fatigue* or gambling or trichotillomania or vaginismus or anhedoni* or affective symptoms or mental disorder* or mental health).ti. 27. (or/1-26) 28. controlled clinical trial.pt. 29. randomized controlled trial.pt. 30. (randomi#ed or randomi#ation).ab,ti. 31. randomly.ab. 32. (random* adj3 (administ* or allocat* or assign* or class* or control* or determine* or divide* or distribut* or expose* or fashion or number* or place* or recruit* or subsitut* or treat*)).ab. 33. placebo*.ab,ti. 34. drug therapy.fs. 35. trial.ab,ti. 36. groups.ab. 37. (control* adj3 (trial* or study or studies)).ab,ti. 38. ((singl* or doubl* or tripl* or trebl*) adj3 (blind* or mask* or dummy*)).mp. 39. clinical trial, phase ii/ or clinical trial, phase iii/ or clinical trial, phase iv/ or randomized controlled trial/ or pragmatic clinical trial/ 40. (quasi adj (experimental or random$)).ti,ab. 41. ((waitlist* or wait* list* or treatment as usual or tau) adj3 (control or group)).ab. 42. (or/28-41) 43. (27 and 42)

OVID EMBASE (1974 to date): 1. eating disorder/ or anorexia nervosa/ or binge eating disorder/ or bulimia/ or female athlete triad/ or food aversion/ or pica/ 2. automutilation/ 3. suicidal behavior/ or self poisoning/ or suicidal ideation/ or suicide/ or suicide attempt/ 4. mania/ or hypomania/ or manic psychosis/ 5. bipolar disorder/ or bipolar depression/ or bipolar i disorder/ or bipolar ii disorder/ or bipolar mania/ or cyclothymia/ or manic depressive psychosis/ or "mixed mania and depression"/ or rapid cycling bipolar disorder/ 6. depression/ or agitated depression/ or atypical depression/ or depressive psychosis/ or dysphoria/ or dysthymia/ or endogenous depression/ or involutional depression/ or major depression/ or masked depression/ or melancholia/ or "mixed anxiety and depression"/ or "mixed depression and dementia"/ or mourning syndrome/ or organic depression/ or postoperative depression/ or premenstrual dysphoric disorder/ or pseudodementia/ or puerperal depression/ or reactive depression/ or recurrent brief depression/ or seasonal affective disorder/ 7. puerperal psychosis/ 8. neurosis/ or affective neurosis/ or anxiety neurosis/ or dysthymia/ or hysteria/ or neurasthenia/ or psychasthenia/ 9. adjustment disorder/ 10. anxiety/ 11. anxiety disorder/ or acute stress disorder/ or anxiety neurosis/ or cardiac anxiety/ or distress syndrome/ or generalized anxiety disorder/ or koro/ or "mixed anxiety and depression"/ or panic/ or posttraumatic stress disorder/ or psychasthenia/ or separation anxiety/ 12. obsessive compulsive disorder/ or compulsion/ or obsession/ 13. phobia/ or agoraphobia/ or claustrophobia/ or homophobia/ or neophobia/ or social phobia/ 14. somatoform disorder/ or body dysmorphic disorder/ or cardiac anxiety/ or conversion disorder/ or delusional pregnancy/ or hypochondriasis/ or masked depression/ or psychogenic pain/ or somatic delusion/ or somatization/ 15. mood disorder/ or affective neurosis/ or affective psychosis/ or blunted affect/ or major affective disorder/ or minor affective disorder/ 16. munchausen syndrome by proxy/ or munchausen syndrome/ 17. psychosexual disorder/ or anorgasmia/ or castration anxiety/ or frigidity/ or koro/ or libido disorder/ or oedipus complex/ or orgasm disorder/ or psychogenic impotence/ or sexual addiction/ or sexual arousal disorder/ or vaginism/ 18. impulse control disorder/ or intermittent explosive disorder/ or kleptomania/ or pathological gambling/

or pyromania/ or trichotillomania/ 19. mental stress/ 20. emotional disorder/ 21. mood disorder/ or affective neurosis/ or blunted affect/ or depression/ or major affective disorder/ or mania/ or minor affective disorder/ 22. (or/1-21) 23. randomized controlled trial.de. 24. randomization.de. 25. placebo.de. 26. placebo$.ti,ab. 27. randomi#ed.ti,ab. 28. randomly.ab. 29. ((singl$ or doubl$ or trebl$ or tripl$) adj3 (blind$ or mask$ or dummy)).mp. 30. factorial$.ti,ab. 31. allocat$.ti,ab. 32. assign$.ti,ab. 33. volunteer$.ti,ab. 34. crossover procedure.de. 35. (crossover$ or cross over$).ti,ab. 36. (quasi adj (experimental or random$)).mp. 37. (control$ adj3 (trial$ or study or studies or group $)).ti,ab. 38. ((animal or nonhuman) not (human and (animal or nonhuman))).de. 39. (or/23-37) 40. (39 not 38) 41. (22 and 40)

OVID PsycINFO (1967 to date): 1. eating disorders/ or anorexia nervosa/ or bulimia/ or hyperphagia/ or kleine levin syndrome/ or pica/ or "purging (eating disorders)"/ 2. aphagia/ 3. coprophagia/ 4. binge eating/ 5. self destructive behavior/ or attempted suicide/ or head banging/ or self inflicted wounds/ or self injurious behavior/ or self mutilation/ or suicide/ 6. suicide prevention/ 7. suicidal ideation/ 8. affective disorders/ 9. affective psychosis/ 10. bipolar disorder/ or cyclothymic personality/ 11. major depression/ or anaclitic depression/ or dysthymic disorder/ or endogenous depression/ or postpartum depression/ or reactive depression/ or recurrent depression/ or treatment resistant depression/ 12. atypical depression/ 13. "depression (emotion)"/ 14. seasonal affective disorder/ 15. anxiety disorders/ or acute stress disorder/ or castration anxiety/ or death anxiety/ or generalized anxiety disorder/ or obsessive compulsive disorder/ or panic disorder/ or posttraumatic stress disorder/ or separation anxiety/ 16. phobias/ or acrophobia/ or agoraphobia/ or claustrophobia/ or ophidiophobia/ or school phobia/ or social phobia/ 17. "debriefing (psychological)"/ 18. neurosis/ or childhood neurosis/ or experimental neurosis/ or occupational neurosis/ or traumatic neurosis/ 19. adjustment disorders/ 20. coping behavior/ 21. adjustment/ or exp emotional adjustment/ or occupational adjustment/ or school adjustment/ or social adjustment/ 22. emotional trauma/ 23. stress/ or chronic stress/ or environmental stress/ or occupational stress/ or psychological stress/ or social stress/ or stress reactions/ 24. anxiety/ or computer anxiety/ or mathematics anxiety/ or performance anxiety/ or social anxiety/ or speech anxiety/ or test anxiety/ 25. panic attack/ or panic/ or panic disorder/ 26. somatoform disorders/ or body dysmorphic disorder/ or hypochondriasis/ or neurasthenia/ or neurodermatitis/ or somatization disorder/ or somatoform pain disorder/ 27. conversion disorder/ or hysterical paralysis/ or hysterical vision disturbances/ or pseudocyesis/ 28. somatization/ 29. hysteria/ or mass hysteria/ 30. hysterical paralysis/ 31. histrionic personality disorder/ 32. malingering/ 33. factitious disorders/ or munchausen syndrome by proxy/ or munchausen syndrome/ 34. chronic fatigue syndrome/ 35. compulsions/ or repetition compulsion/ 36. obsessions/ 37. obsessive compulsive personality disorder/ 38. trichotillomania/ 39. gambling/ or pathological gambling/ 40. sexual function disturbances/ or dyspareunia/ or erectile dysfunction/ or female sexual dysfunction/ or inhibited sexual desire/ or premature ejaculation/ or vaginismus/ 41. premenstrual dysphoric disorder/ 42. *mental disorders/ 43. (eating disorder* or anorexi* or bulimi* or binge eat* or (self adj (injur* or mutilat*)) or suicide* or suicidal or parasuicid* or mood disorder* or affective disorder* or bipolar i or bipolar ii or (bipolar and (affective or disorder*)) or mania or manic or cyclothymi* or depression or depressive or dysthymi* or neurotic or neurosis or adjustment disorder* or antidepress* or anxiety disorder* or agoraphobia or obsess* or compulsi* or panic or phobi* or ptsd or posttrauma* or post trauma* or combat or somatoform or somati#ation or medical* unexplained or body dysmorphi* or conversion disorder or hypochondria* or neurastheni* or hysteria or munchausen or chronic fatigue* or gambling or trichotillomania or vaginismus or anhedoni* or affective symptoms or mental disorder* or mental health).ti,id. 44. (or/1-43) 45. treatment effectiveness evaluation.sh. 46. clinical trials.sh. 47. mental health program evaluation.sh. 48. placebo.sh. 49. placebo$.ti,ab. 50. randomly.ab. 51. randomi#ed.ti,ab. 52. trial$.ti,ab. 53. ((singl$ or doubl$ or trebl$ or tripl$) adj3 (blind$ or mask$ or dummy)).mp. 54. (control$ adj3 (trial$ or study or studies or group$)).ti,ab. 55. "2000".md. 56. factorial$.ti,ab. 57. allocat$.ti,ab. 58. assign$.ti,ab. 59. volunteer$.ti,ab. 60. (crossover$ or cross over$).ti,ab. 61. (quasi adj (experimental or random$)).mp. 62. ((waitlist* or wait* list* or treatment as usual or tau) adj3 (control or group)).ab. 63. (random* adj3 (administ* or class* or control* or determine* or divide* or distribut* or expose* or fashion or number* or place* or recruit* or subsitut* or treat*)).ab. 64. (or/45-63) 65. (44 and 64)

CONTRIBUTIONS OF AUTHORS

Cindy-Lee Dennis developed the protocol.

Hilary Brown and Jennifer Brown assisted Cindy-Lee Dennis with the development of the protocol.

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Cindy-Lee Dennis: none known

Hilary K Brown: none known

Jennifer VE Brown: none known

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